Via Facsimile
Date of Deposit: July 22, 2004

Attorney Docket No: 21629-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Hoffman, Andrew		
SERIAL NUMBER:	09/616,483	EXAMINER:	Patel, Mital B.
FILING DATE:	July 14, 2000	ART UNIT:	3761
FOR:	DRUG DELIVERY DEVICE FOR ANIMALS		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF PRIOR INVENTION UNDER 37 C.F.R. § 1.131

I, Ingrid A. Beattie, declare:

1. I am the patent counsel to Tufts University, assignee of the above-referenced patent application.
2. I submit herewith a copy of billing records to establish diligence in working to constructive reduction to practice of the claimed invention from a time prior to the May 16, 2000 effective filing date of Barney et al. to the July 14, 2000 filing date of the above-referenced patent application.
3. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Title 18, United States Code, § 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

IABeattie
Declarant's Signature

July 22, 2004
Date

Full Name of Declarant: Ingrid A. Beattie

Attachments:
Exhibit: Invoice # 8147170

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TUFTS UNIVERSITY
THOMAS J. MCVARISH
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136 HARRISON AVENUE
BOSTON, MA 02111

August 10, 2000
Invoice # 8147170
Client # 21629

FOR PROFESSIONAL SERVICES RENDERED THROUGH JULY 31, 2000

RE: 09/616483 DRUG DELIVERY DEVICE FOR ANIMALS

21629-001

05/[redacted]/00	Review prior art.	I A BEATTIE	[redacted]
05/[redacted]/00	Meeting with Dr. Hoffman; review prior art references; work on application.	I A BEATTIE	[redacted]
06/15/00	Work on application.	I A BEATTIE	[redacted]
06/25/00	Work on application.	I A BEATTIE	[redacted]
06/27/00	Work on application.	I A BEATTIE	[redacted]
06/28/00	Work on application.	I A BEATTIE	[redacted]
06/30/00	Work on application.	I A BEATTIE	[redacted]
07/03/00	Work on application.	I A BEATTIE	[redacted]
07/08/00	Work on application; send claims to client.	I A BEATTIE	[redacted]
07/10/00	Work on application.	I A BEATTIE	[redacted]
07/12/00	Telephone conference with F. Toneguzzo regarding claim strategy.	I A BEATTIE	[redacted]

:UFTS UNIVERSITY
:LIENT NUMBER: 21629
:NVOICE NO.: 8147170

August 10, 2000 PAGE 2

)7/14/00	Work on and file application; telephone conference with Dr. Hoffman.	I A BEATTIE	[redacted]
)7/25/00	Attention to email form Dr. Hoffman regarding status of patent application.	I A BEATTIE	[redacted]

TOTAL MATTER SERVICES: [redacted]

MATTER EXPENSE SUMMARY

Reprographics	[redacted]
Evening/WP Secretarial Time	
Postage	
Telephone	
Filing Fees - -FOR- 7/14/00 (USPTO/UTILITY APPLICATION)	

TOTAL MATTER EXPENSES: [redacted]

TOTAL MATTER FEES AND EXPENSES: [redacted]

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Fax Cover Sheet

DATE: July 22, 2004

FROM: Ingrid A. Beattie, Ph.D., J.D.
Direct Dial 617 348 1838
iabeattie@mintz.com

TO:

NAME	BUSINESS #	FAX #
Examiner Mital B. Patel		703 746-3388

MESSAGE:

Applicant: **Hoffman, Andrew**
U.S. Serial No.: **09/616,483**
Filing Date: **July 14, 2000**
Title: **DRUG DELIVERY DEVICE FOR ANIMALS**

Attached, please find the following documents:

1. Supplemental Response;
2. Declaration of Prior Invention of Andrew Hoffman;
3. Declaration of Prior Invention of Ingrid A. Beattie, Ph.D., J.D.;
4. Invoice No. 8147170

1. Exhibit A (Hoffman Decl.) 3 pages

2. Exhibit B (Hoffman Decl.) 4 pages

Please call me with any questions.

Ingrid A. Beattie, Ph.D., J.D.

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We are sending a total of pages, including this cover sheet.

Please call us at 617 654 8024, if you experience any problems.

[redacted] 11:57 TUFTS ASSOC. PROVOST/RES. 617 636 2917 P.08/11

MAINLY I. USES

A HOFFMAN [redacted]

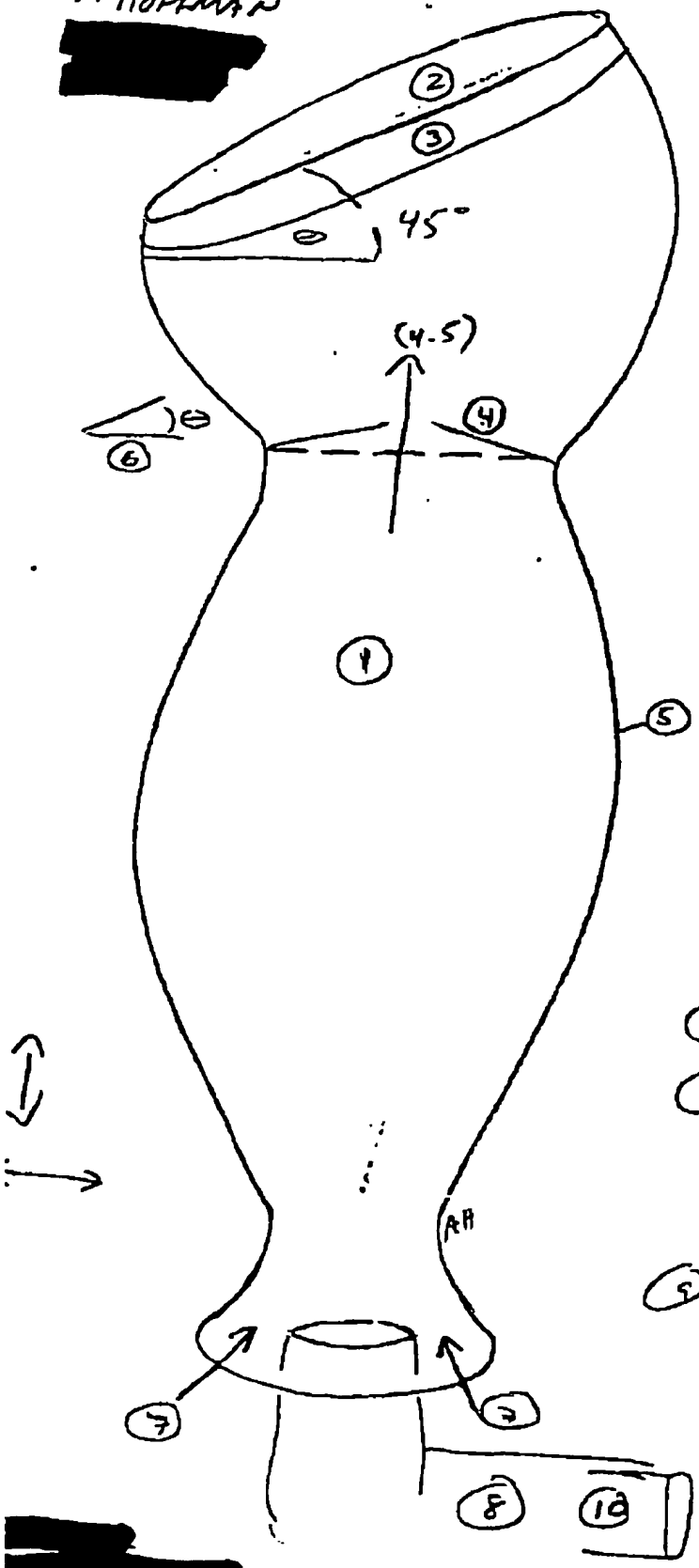


Fig 1

(1) SPACER HOLDING CHAMBER

(2) OPENING WHICH FITS OVER NARIS (CIRCULAR OPENING)

(3) SOFT RUBBER-LIKE INTERFACE

(4) INSPIRATORY VALVE (< 0.05 cm H_2O / L/sec)

(4.5) UNIDIRECTIONAL FLOW triggered by inspiration

NOTE: EXPIRATORY FLOW OCCURS THROUGH OPPOSITE NOSTRIL OR BY REMOVING DEVICE

(5) CLEAR SYNTHETIC PLASTIC MATERIAL – PREFERABLY NON-ELECTROSTATIC.

(6) APPROXIMATE MINIMUM ANGLE – ALLOWS PERSON TO STAND IN VARIOUS POSITIONS FOR DELIVERY (45° is recommended)

(7) LOW RESISTANCE INTAKES (< 0.05 cm H_2O/L/sec)

(8) pMDI, DPI or other DRUG & DRUG DELIVERY SYSTEM UPSCALED IN SIZE FOR HORSES.

(9) DIMENSIONS COULD VARY

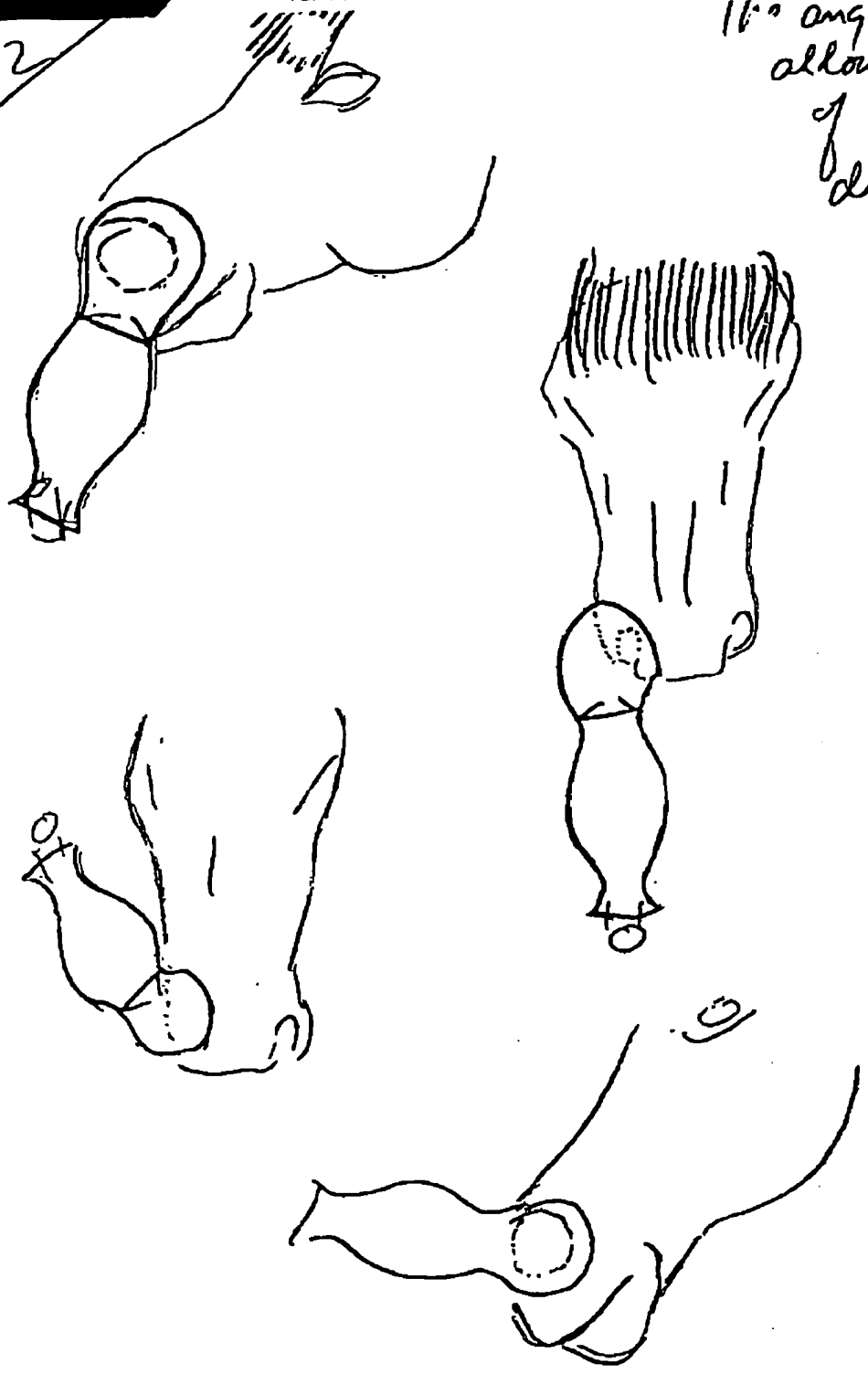
(10) EXAMPLES OF PER-ACTUATION DOSES

ALBUTEROL 450 mcg, 200 µg
IPRATROPIUM-Br 90 mcg
FLUTICASONE 1.1 mg, 50 µg
BECLOMETHASONE 250 µg - SUMMER

[redacted]

[redacted]

Fig 2



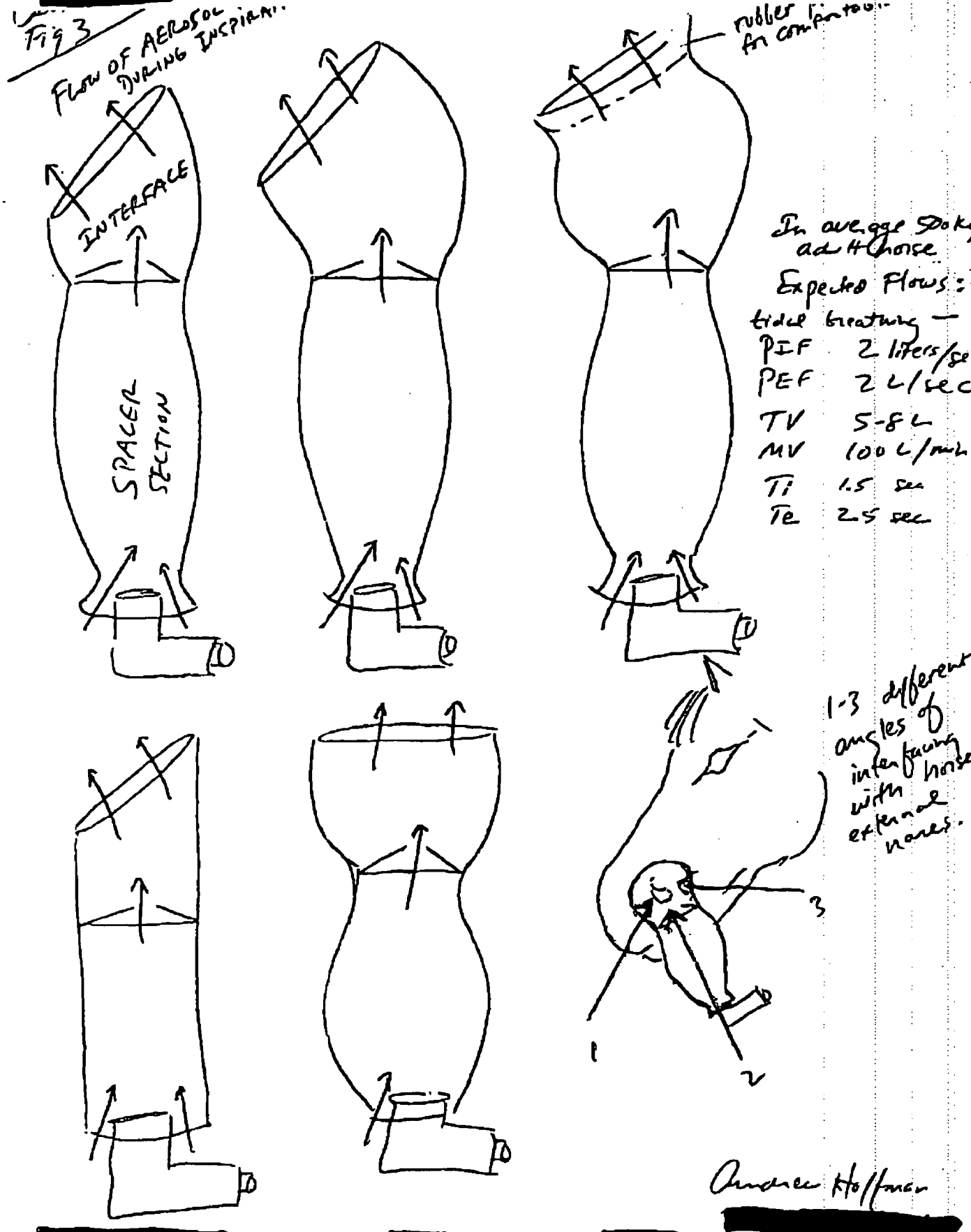
11° angled interface allows for a variety of positions during administration of inhaled drugs.

Exhibit A (2 of 3)

Alto Ffman [redacted]

[redacted] 11:58 TUFTS ASSOC. PROVOST/RES.

Fig 3



Andrea Hoffman

[redacted]

Compact inhalation drug delivery device for animals

Dr. Andrew Hoffman
Tufts University School of Veterinary Medicine
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North Grafton, MA, 01536, USA

[redacted]

Background

Small airway diseases (i.e. including small airway inflammatory disease, heaves, chronic obstructive pulmonary disease) are prevalent causes of exercise intolerance, cough, and asthma-like attacks in horses (Hoffman 1997). These clinical signs are thought precipitated by progressive allergic reactions to dust found in hay and in the environment, but the cause is not always identified. Traditional management includes minimizing the horse's exposure to dust and conventional hay, bronchodilator treatment for immediate relief, steroid treatment to reduce inflammation and bring about remission, and long-term preventative control with inhaled anti-inflammatories (Hoffman 1993, 1997, 1999, Rush 1998, 1999, Ammann 1998). More recently, there are studies that demonstrate the efficacy of inhaled medications for treatment of small airway diseases (Hoffman 1993, Tesarowski 1994, Derksen 1996). The advantage of using aerosols for treatment over using oral or parenteral drugs, is the fact that aerosols treat the airways directly and topically, with little systemic (i.e. blood) absorption (Hoffman 1997). As a result, there are little to no side effects caused by aerosols, yet a potent effect on the target tissues, the airways.

To deliver aerosols to the lung without voluntary cooperation from a horse is a special consideration. To date, two methods have been developed. The first method (Hoffman 1993, Tesarowski 1994) involves the placement of a facemask, with one

Exhibit B (1 of 4)

unidirectional inhalation valve mounted on the proximal end, and two exhalation (i.e. exit) valves mounted on the side of the mask ("Equine Mask with MDI Adapter" US Patent 5,954,049, Sept 21,1999). A spacer chamber ("MDI Adapter") is placed over the inhalation valve, allowing for the horse to inhale the aerosol from the chamber. This device is most suitable for delivery of aerosols from pressurized cannisters (pMDI). Effectively, this device prevents drug, actuated into the chamber, from being exhaled out the chamber. This permits unidirectional flow of the drug from the chamber, to the mask, and finally the respiratory system via the nasal passages, without the need for coordinating the timing of pMDI actuation and inhalation. In summary, the advantage of this device is that it offers "virtual breath actuation", is easily cleaned, and only requires that a mask is placed on the muzzle of the animal. A second system that has been patented recently ("Attachment for Aerosol Device for Large Animals and Method of Use", US Patent 5,666,948, Sept 16, 1997) requires that the actuation of the pMDI is coordinated with inspiration (Derksen 1996). The drug is actuated through a bulb and stem, which acts like a holding chamber, and is placed within one nostril, pointing distally. The drug is inhaled with air that flows through the bulb-stem chamber during inhalation. The advantage of the latter system may be greater deposition, since the external nares are bypassed. The disadvantage of the latter system is the need to place the device in the nose, and the tendency for asynchrony between the actuation of the cannister and the animal's inhalation, resulting in drug wastage.

A device that does not require insertion in the nose is desirable from the perspective of the animal, since nasal insertion is irritating, and the owner, that is upset having to place this device in their animal's nose, is also required to perform more

Exhibit B (2 of 4)

rigorous restraint. Furthermore, not all horses will accept this device initially. A device that is more compact than Patent 5,954,049 would also be advantageous, since carrying the device on trail rides, and storage space can be limited. The following description is of a device that combines the advantages of compactness and does not require insertion into the nose, while preserving the desired effect. Preliminary studies with external nasal delivery of bronchodilator aerosols in horses have demonstrated beneficial effects as for the mask device (unpublished data).

Description of the inventions (Devices 1 and 2)

The devices are composed of clear solid plastic or similar material, with minimal electrostatic properties. There are two possible arrangements envisaged. Device 1 is larger and incorporates a holding chamber. The size and features of Device 1 are approximately depicted in Fig 1. Device 1 is applicable to delivery of pMDI aerosols, since these require a spacer chamber for holding the drug in a cloud suspension prior to inhalation. A one-way valve is used to separate the holding chamber from a patient interface, which is angled to allow the user to stand off to the side, yet minimize the angle of delivery and therefore maximize deposition in the respiratory system. Device 1 has small holes on the proximal (pMDI) end, which allow air to flow through the chamber to evacuate the drug into the respiratory system during inhalation. On the distal end, the interface mushrooms to cover the nare on one side (either side) of the horse. The circular opening allows for a number of angles of attachment (Fig 2 and 3). The interface may have a soft rubber or latex boot for comfort and better conformation to the individual's shape. The inspiratory valve creates very little resistance (< 1 cm H_2O), to

Exhibit B (3 of 4)

afford maximal opening during inspiration. Expiratory flow is through the opposite nostril, so the inhaler can stay on the face as long as desired without interruption of breathing or drub deliveries. Device 1 could be used for delivery of dry powders or flow-though powders or flow-actuated aerosols of any type.

The second device (Device 2) is one that does not require a holding (i.e. spacer) chamber, and therefore is a collapsed version of Device 1. There is no inhalation valve, since the drug is swept with flow through the drug cannister. The drug cannisters used must possess this flow-through characteristic. This could apply to dry powder or propellant-based flow-through drug cannisters. There is no need for holes in the proximal end to accommodate flow in Device 2, since it is desirable to divert flow through the drug cannister. Device 2 is simply pressed against the nares, and with the next inhalation, a dose of the drug exits the cannister, into a short plastic interface space, and quickly from there into the horse during inhalation. This can be repeated on the next inhalation without delay. Again exhalation can be achieved through the opposite nostril, or by removing the device. Device 2 is super compact, and highly efficient, since it requires only normal breathing and no drug is wasted in a holding chamber. As there there is no significant delay in delivery (i.e. the drug is delivered directly from cannister to patient), there would be little chance of losing drug to evaporation or environmental degradation. The horse can not exhale through the chamber, since there is no flow permitted in this direction.

The devices described here are not limited to the designs in this description, in that there can be variation as to size, angulation of the interface, materials, and dimensions. Furthermore, their use would not be limited to use in horses. [redacted]

Exhibit B (4 of 4)